IMPEL NEUROPHARMA TO PRESENT PIVOTAL, PHASE 3 DATA FROM STOP-301
STUDY AT THE 63RD ANNUAL MEETING OF THE AMERICAN HEADACHE SOCIETY

Data Will Evaluate Exploratory Efficacy Data from STOP-301 Study Evaluating INP104 Consistency of Response, Recurrence and Sustained Response

Findings Also Highlight Safety and Tolerability Including Nausea and Nasal and Cardiovascular Safety as a Promising Potential New Option for the Treatment of Acute Migraine Attacks

SEATTLE, June 2, 2021 — Impel NeuroPharma, a late-stage biopharmaceutical company focused on the development and commercialization of transformative therapies for patients living with central nervous system (CNS) diseases with high unmet medical needs, announced today that it will present data from eight scientific abstracts at the 63rd American Headache Society Annual Scientific Meeting (AHS), taking place virtually from June 3 – 6, 2021.

Investigational INP104 is dihydroergotamine mesylate (DHE) delivered directly into the vascular-rich upper nasal space using Impel’s proprietary Precision Olfactory Delivery (POD®) technology. Many current nasal delivery technologies – sprays, droppers, and pumps – may deliver less than 5% of the active drug to the upper nasal space.1

“We are proud to share data that further strengthens the INP104 safety, tolerability and exploratory efficacy profile and builds upon evidence that it may be a promising new acute treatment for migraine attacks, offering consistent and sustained relief,” said Stephen Shrewsbury, M.D., Chief Medical Officer at Impel NeuroPharma. “By delivering optimal doses of DHE—a well-established and effective migraine therapy—into the upper nasal space, INP104 leverages an untapped gateway for treatment administration that could benefit absorption and migraine relief, especially among people with migraine who have comorbid gastrointestinal disorders, whether symptomatic or not.”

Impel will share data from its pivotal Phase 3, open-label “STOP-301” study evaluating INP104 for the acute treatment of migraine, including patient-reported exploratory efficacy findings for pain and most bothersome symptom relief and freedom regarding consistency and sustainability of response and migraine recurrence. STOP-301 safety and tolerability data presentations will include findings on nausea, as well as nasal and cardiovascular safety. STOP-301 is a Phase 3, pivotal, open-label trial evaluating the safety, tolerability, and exploratory efficacy of INP104. Additionally, Impel will present a literature review regarding DHE pharmacology and DHE’s broad receptor profile.

“A high percentage of people with migraine experience nausea, vomiting and other gastrointestinal symptoms. Among these people, there is variability in absorption of oral medications,” said Carrie Dougherty, MD, FAHS, Associate Professor of Neurology at MedStar Georgetown University Hospital. “This novel delivery, targeting the upper nasal space, has the potential to have a significant advantage in the management of migraine.”
STOP-301 data presented at AHS includes:

- A post-hoc analysis found that INP104 treatment showed high levels of consistency across multiple migraine attacks over 24 weeks.
  - **Presentation Title:** Treatment Consistency Across Multiple Migraine Attacks: Results from the Phase 3 STOP 301 Open-Label Study
  - **Abstract Number:** 1001404

- A single dose of INP104 was associated with high rates of sustained efficacy for those who had obtained relief with INP104 for their first treated migraine. In addition, the data found that treatment with INP104 was associated with low rates of migraine recurrence.
  - **Presentation Title:** Recurrence Rates for INP104 for the Acute Treatment of Migraine: Results from the Phase 3 STOP 301 Open-Label Study
  - **Abstract Number:** 1001469

- Of the 6,332 doses of INP104 administered, less than 1% of doses were reported to result in nausea. The majority of reported instances of nausea were mild to moderate in severity.
  - **Presentation Title:** Reduced Nausea When Dihydroergotamine Mesylate Is Delivered by INP104
  - **Abstract Number:** 1001405

- In the absence of a direct comparison, results suggest that INP104 was associated with high rates of symptom freedom and may be a promising new acute treatment for migraine.
  - **Presentation Title:** Acute Treatment of Migraine with INP104: Exploratory Efficacy from the STOP 301 Phase 3 Study
  - **Abstract Number:** 1001475

- No significant adverse events were noted in the peripheral or cardiovascular (CV) system, even in patients with CV risk factors or concomitant triptan use.
  - **Presentation Title:** Cardiovascular Safety Results of INP104 (POD-DHE) from the STOP 301 Phase 3 Study
  - **Abstract Number:** 1001476

- Over 90% of patients had normal upper nasal endoscopies reported throughout the 24-week trial. Mild to moderate edema was observed in the nasal mucosal, but was not considered a concerning finding.
  - **Presentation Title:** Nasal Safety of Chronic Intermittent Use of INP104: Results from the Phase 3 STOP 301 Open-Label Study
  - **Abstract Number:** 1001356

In addition to STOP-301 data, Impel will also present:
• A literature review of new and existing migraine-specific treatments, which found that compared to other therapies, DHE displays a broad range of pharmacological activity across multiple receptors, including serotonergic (5-HT), adrenergic (α), and dopaminergic (D) receptor subtypes, therefore exerting a greater influence over the pathophysiology of the migraine cycle.
  o Presentation Title: DHE Pharmacology revisited: Does a broad receptor profile molecule treat the whole migraine?
  o Abstract Number: 1001481

• A study comparing clinical outcomes of INP104 versus gepants and DHE nasal spray by an industry standard matching-adjusted indirect comparison (MAIC). The study found INP104 was associated with greater reductions in pain and other migraine-related symptoms in indirect comparison with gepants.
  o Presentation Title: Assessing the Comparative Efficacy of INP104 For Acute Treatment Of Migraine Attacks: A Matching-Adjusted Indirect Comparison

The New Drug Application (NDA) for INP104 was accepted for review by the U.S. Food and Drug Administration (FDA) in January 2021 and has a Prescription Drug User Fee Act (PDUFA) target action date of September 6, 2021. If approved by the FDA, INP104 will become the first and only therapy to deliver DHE to the vascular-rich upper nasal space using the POD technology, a novel delivery system. The FDA has conditionally accepted a trade name of TRUDHESA™.

All presentations will be accessible on the AHS website at https://www.americanheadachesociety.org/. Presentation details are highlighted below.

About STOP-301:
STOP-301 was a pivotal, Phase 3 open-label study that evaluated the safety, tolerability, and exploratory efficacy of INP104. The trial enrolled 360 patients at 36 sites in the United States who had a documented diagnosis of migraine with or without aura, with at least two attacks per month for the previous six months. The study evaluated 6,332 doses of INP104.

In the trial, 354 patients received at least one dose of INP104 and comprised the 24-week Full Safety Set. Of the 185 patients who took an average of two or more treatments with INP104 per 28-day period during the 24-week treatment period comprised the Primary Safety Set. Of those enrolled, 74% (n=262) of patients completed the 24-week treatment period. A subset of 73 patients continued into a 28-week treatment extension period to 52 weeks total, of which 90% completed.

About Precision Olfactory Delivery or POD® Technology:
Impel’s proprietary Precision Olfactory Delivery (POD®) technology is able to deliver a range of therapeutic molecules and formulations into the vascular-rich upper nasal space, believed to be a gateway for unlocking the previously unrealized full potential of these molecules. By delivering predictable doses of drug directly to the upper nasal space, Impel’s precision performance technology has the goal of enabling increased and consistent absorption of drug, overriding the high variability associated with other nasal delivery systems, yet without the need for an injection. While an ideal target
for drug administration, to date no technology has been able to consistently deliver drugs to the upper nasal space. By utilizing this route of administration, Impel NeuroPharma has been able to demonstrate blood concentration levels for its investigational therapies that are comparable to intramuscular (IM) administration and can even reach intravenous (IV)-like systemic levels quickly, which could transform the treatment landscape for CNS and other disorders. Importantly, the POD technology offers propellant-enabled delivery of dry powder and liquid formulations that eliminates the need for coordination of breathing, allowing for self- or caregiver-administration in a manner that may improve patient outcome, comfort, and potentially, compliance.

**About Migraine and About the Acute Treatment of Migraine:**
Migraine is a common and debilitating neurological disease characterized by recurrent episodes of severe head pain and associated with nausea, vomiting and sensitivity to light and sound. 2 Migraine affects approximately 36 million people in the United States. 3 Of the approximately 18 million diagnosed migraine patients, only four million are on prescription treatment. 4 While triptans account for almost 80 percent of migraine therapies, approximately 30 to 40 percent of patients do not respond adequately to triptans and up to 79 percent of the patients who do respond to triptans report being dissatisfied with their current treatment and willing to try a new therapy. 5,6,7 Further, evidence suggests that gastroparesis, delayed emptying of the stomach, is a prevalent feature in migraine that may delay or reduce the absorption of oral medications, including triptans, gepants and ditans. This means that acute medications can remain in the stomach for hours, delaying symptom relief, leading to loss of confidence (about future administration) and prolonged suffering for the current migraine attack. 8

**About Impel NeuroPharma:**
Impel NeuroPharma, Inc. is a late-stage pharmaceutical company focused on utilizing its proprietary technology to develop and commercialize transformative therapies for people suffering from diseases with high unmet needs, with an initial focus on diseases of the CNS. The Company’s strategy is to rapidly advance its product candidate pipeline that pairs its proprietary Precision Olfactory Delivery (POD®) system with well-established therapeutics, including INP104 for the acute treatment of migraine, INP105 for the acute treatment of agitation in patients with autism, and INP107 for OFF episodes in Parkinson’s disease.

**Cautionary Note on Forward-Looking Statements**
This press release contains “forward-looking” statements within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995, including, but not limited to, timing of approval of Impel’s NDA for INP104 (proposed trade name TRUDHESA™) and of Impel’s other regulatory submissions, timing of announcements of clinical results and clinical development activities of its product candidates, potential benefits and market opportunities of INP104 and its other product candidates and its cash runway. Forward-looking statements can be identified by words such as: “believe,” “may,” “will,” “potentially,” “estimate,” “continue,” “anticipate,” “intend,” “could,” “would,” “project,” “plan,” “expect” or the negative or plural of these words or similar expressions. These statements are subject to numerous risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including but not limited to, Impel’s ability to obtain and maintain regulatory approval of INP104 and its other product candidates, its ability to execute its commercialization strategy for INP104 its ability to develop, manufacture and commercialize its product candidates including plans for future
development of its POD devices and plans to address additional indications for which Impel may pursue regulatory approval, whether results of preclinical studies or clinical trials will be indicative of the results of future trials, and the effects of COVID-19 on its clinical programs and business operations. Many of these risks are described in greater detail in Impel’s filings with the Securities and Exchange Commission. Any forward-looking statements in this press release speak only as of the date of this press release. Impel assumes no obligation to update forward-looking statements whether as a result of new information, future events or otherwise, after the date of this press release.

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